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Capt. Steve Lewis, MC, USN

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Status report covers progress made through the period

October 1, 1990 through January 31, 1991

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P.I. Harvey I Miller, Ph.D.

Louisiana State Univ. Medical Center,
New Orleans.

Metabolic Changes and Hemodynamic Dysfunction Following Hypothermic Shock

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Harvey I Miller, Ph.D. - Principal Investigator

STATUS REPORT

From October 1, 1990 To January 31, 1991

Shock, which is the result of acute and severe accidental hypothermia, can produce subtle injuries to several organs. The manifestations of these injuries are difficult to observe because of compensatory mechanisms, however, they can persist many hours past the return to normal body temperature. The severity of these organ dysfunctions is not always great but coupled with other changes can jeopardize the survival of the victim. The purpose of these investigations is to uncover the mechanisms which produce the dysfunctions and determine proper therapeutic procedures to stop and reverse this pathological process. One of the therapeutic interventions which is being studied is fluid resuscitation, which is applied during the short rewarm period. We have shown that following hypothermia and rewarm a cardiac dysfunction persists over 48 hours. This dysfunction is hidden in the whole intact animal because of the cardiovascular compensatory mechanism. However, if the heart is isolated and perfused, hearts from hypothermic animals exhibit flat Starling curves. In other words, hearts from these hypothermically shocked animals lose their physiologic reserve. The question is, "Does the composition and volume of the resuscitation fluid affect the development of the cardiac dysfunction?"

Progress was made in comparing the effect of various resuscitation fluids on the development of cardiac dysfunction in hypothermic shock.

Guinea pigs, with indwelling carotid artery and jugular vein catheters, were anesthetized with Brevitol®, a fast acting barbiturate. When fully narcotized and unconscious, the animals were immersed in an ice-distilled water bath. Core temperature changes were monitored from a second carotid catheter, containing a microthermistor which had been maneuvered into the thoracic aorta. Observations were made and samples collected before the animals were cooled, when the body temperature reached its lowest temperature (22°C-23.5°), when the body temperature returned to 38.5°C (NBT) and at 1,2,3,4 and 24 + 48 hours after reaching its Normal Body Temperature (NBT). Cardiac output, using thermal dilution technique, heart rate and blood pressure were recorded at each time point. A blood sample (0.5 ml) was also collected. Free fatty acids, glucose and lactic acid were determined from the blood samples. Fluid resuscitation was started as soon as the animals were removed from the ice-bath and stopped when the temperature reached NBT. The infusate was <u>not</u> heated. The infusion rate was 0.25 ml/min. There were four groups: a non-resuscitated (NR), a normal saline (.85%) (NS), a Ringers lactate (RL) and a Ringers acetate (RA) solution.

Table I shows the percent change of the cardiac output when normalized to the pre-anesthetized precooled value. All groups had about 15% decrease of the cardiac output at NBT (O time), except NR which had little or no change. At 1 hr post NBT, the Ringers acetate group (RA) and the non resuscitated (NR) group dropped to about 25% while the Ringers lactate group (RL) appeared elevated. The saline group fell to 33% of the precooled level. At 3 and 4 hours the saline group continued to fall while the other groups had a slight increase. Twenty-four hours post cooling, the cardiac output of all groups returned to precool values except saline which continued to be depressed.

After an initial rise during cooling, the mean arterial blood pressure (MABP) fell some 30% of the precooled values at NBT (O time) in all groups. At 1,2 and 3 hours post NBT all resuscitated groups were no different than the precooled controls. The non resuscitated (NR) was depressed as much as 30%. All groups were depressed four hours post recovery, except the Ringers lactate which was not significantly different from the precooled controls. While there was no clear trend of changes in the resuscitated groups at 24 and 48 hours post recovery, the NR was still depressed.

In most types of shock, blood glucose levels are elevated. This was also seen in hypothermic shock when all groups exhibited increases (Table III), peaking at O time. They fell to precooled control values by 2 hours. The NR and RA remained at control levels at 4 hours while NS and RL were depressed. Blood glucose concentration in all groups were elevated 24 and 48 hours post cooling.

Since blood lactate levels are very labile, it is not surprising that this concentration is elevated in all groups, but its elevation is variable. At 1 hour post recovery, the blood lactic acid concentration fell in all groups. Remember, fluid resuscitation was stopped at "O" time when the body temperature returned to normal (NBT). At 4 hours NS and RA did not change from the previous samples while RL and NR appeared to be elevated. At 24 and 48 hours while slightly elevated, there were no differences of lactate concentration between the groups. Because the initial lactate levels are low, 8.1 mg/dl, small changes are magnified. A 50% change in lactate is only an increase to 12 mg/dl.

All groups exhibited general increase in plasma free fatty acid (FFA) except RA. RA showed a slight elevation during 4 hours post recovery and no change from controls at 24 and 48 hours. At 4 hours RL and NR were elevated over 150%. NS was increased somewhat less.

At 24 hours all were no different than controls except NR which remained elevated. Forty-eight hours post recovery all lactate FFA were at or less than control levels.

It is our thesis that even a brief exposure of myocytes to high levels of lactate during shock periods brings about the cardiac dysfunction we observed. We have not clearly observed the cardiac dysfunction in the whole animal following hypothermic shock because of the hemodynamic compensatory mechanisms. We could not relate changes in cardiac output to the nature of the resuscitation fluid nor did the MABP show any difference. The metabolic changes were clearer. The lactate levels were higher and remained elevated in RL and NR at 4 hours. This may be when the damage is done. The elevated FFA may reflect the stress the animals are in at that time. Both lactate and FFA may in part contribute to the cardiac dysfunction. The lactate and FFA in RA and NS seem to be lower and that may be why they recover better. We are now following the development of the dysfunction using the isolated perfused working heart preparation, using hearts from each group at various time periods. This would be especially important at 4 hours post recovery (NBT), when the lactate and FFA are the highest.

NAVAL3.WP

TABLE I

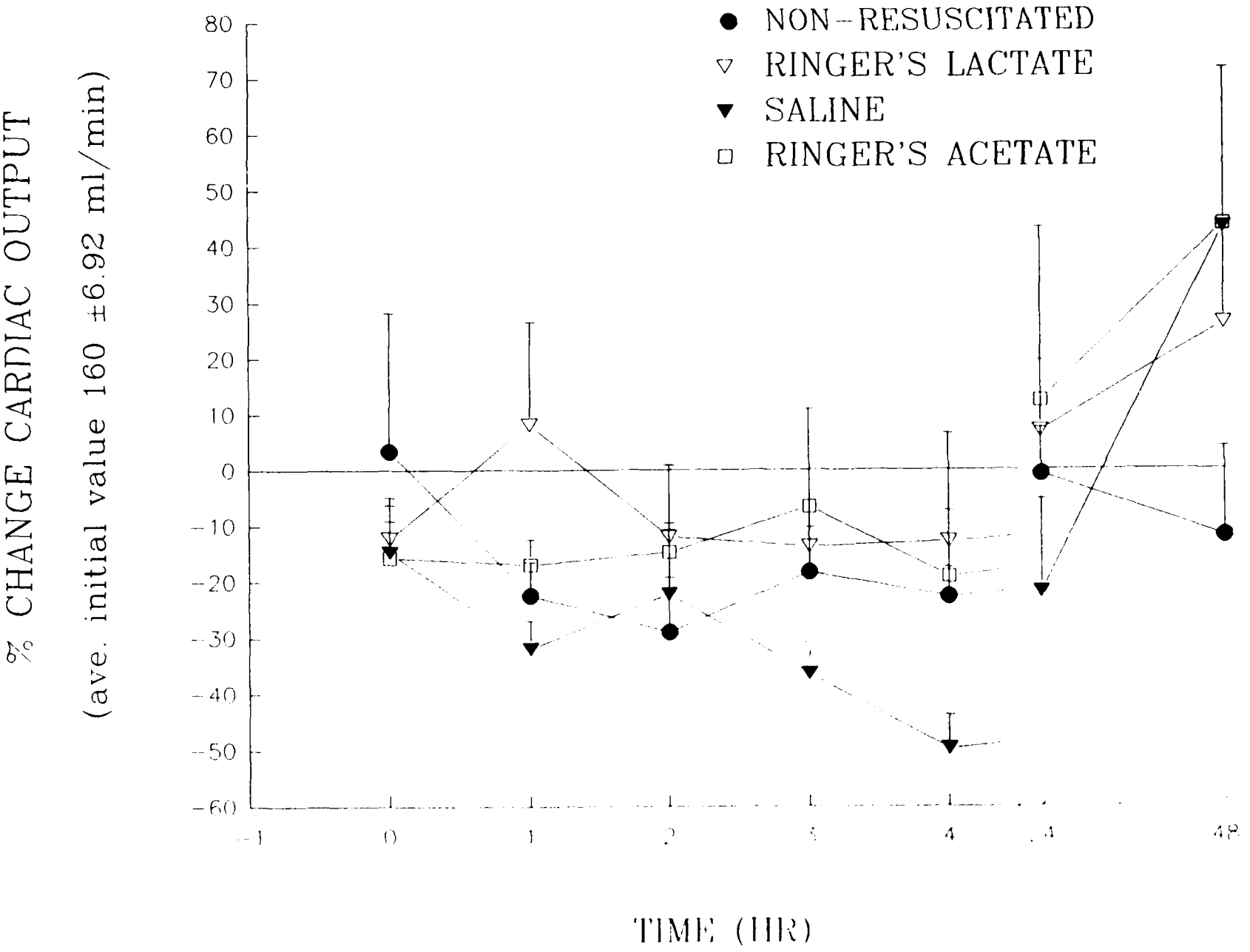

% CHANGE CARDIAC OUTPUT
(ave. initial value 160 ±6.92 ml/min)
NON-RESUSCITATED
RINGER'S LACTATE
SALINE
RINGER'S ACETATE
80
70
60
50
40
30
20
10
0
-10
-20
-30
-40
-50
-60
-1
0
1
2
3
4
24
48
TIME (HR)

TABLE II

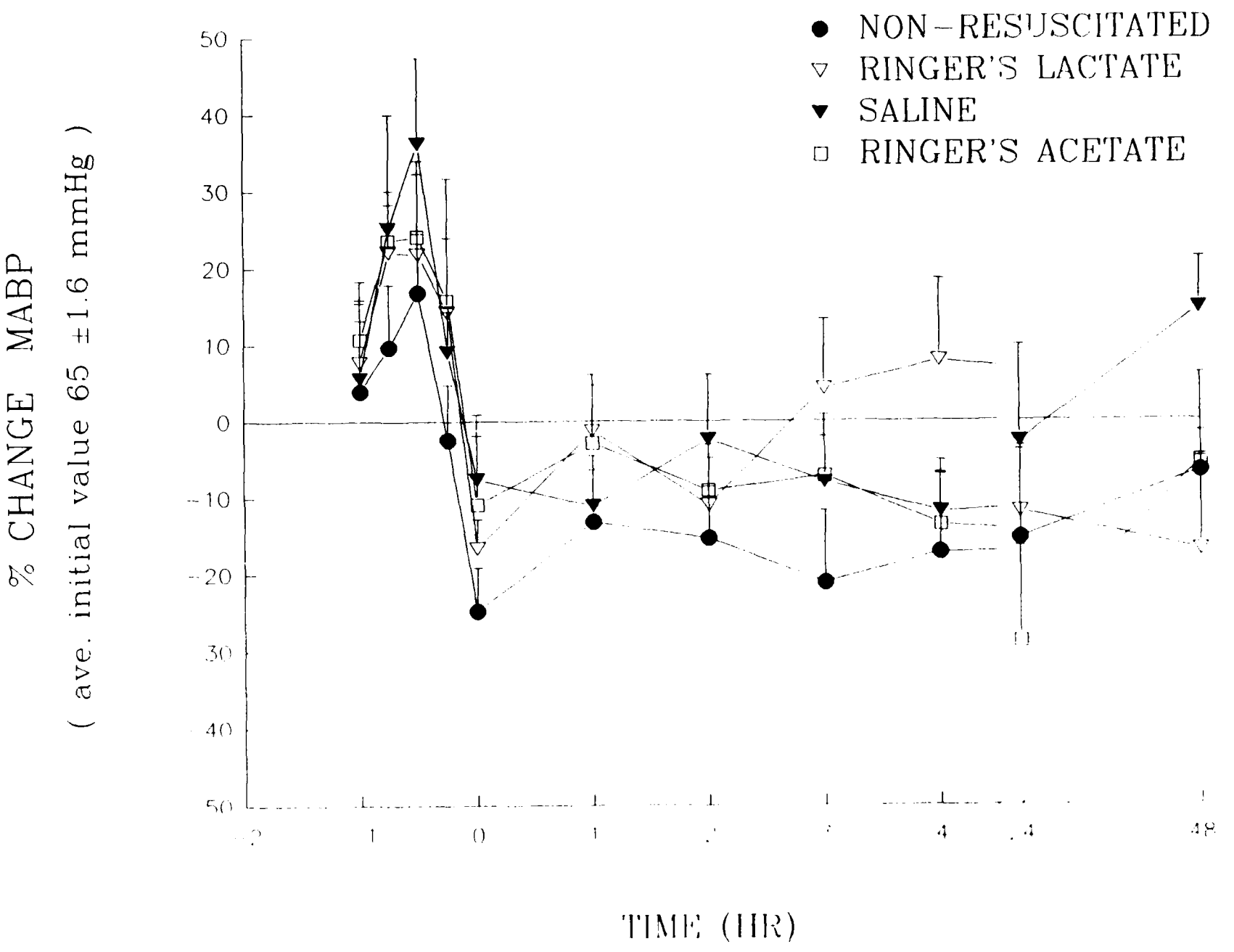

NON-RESUSCITATED
RINGER'S LACTATE
SALINE
RINGER'S ACETATE
% CHANGE MABP
(ave. initial value 65 ±1.6 mmHg)
50
40
30
20
10
0
-10
-20
-30
-40
-50
TIME (HR)

TABLE III

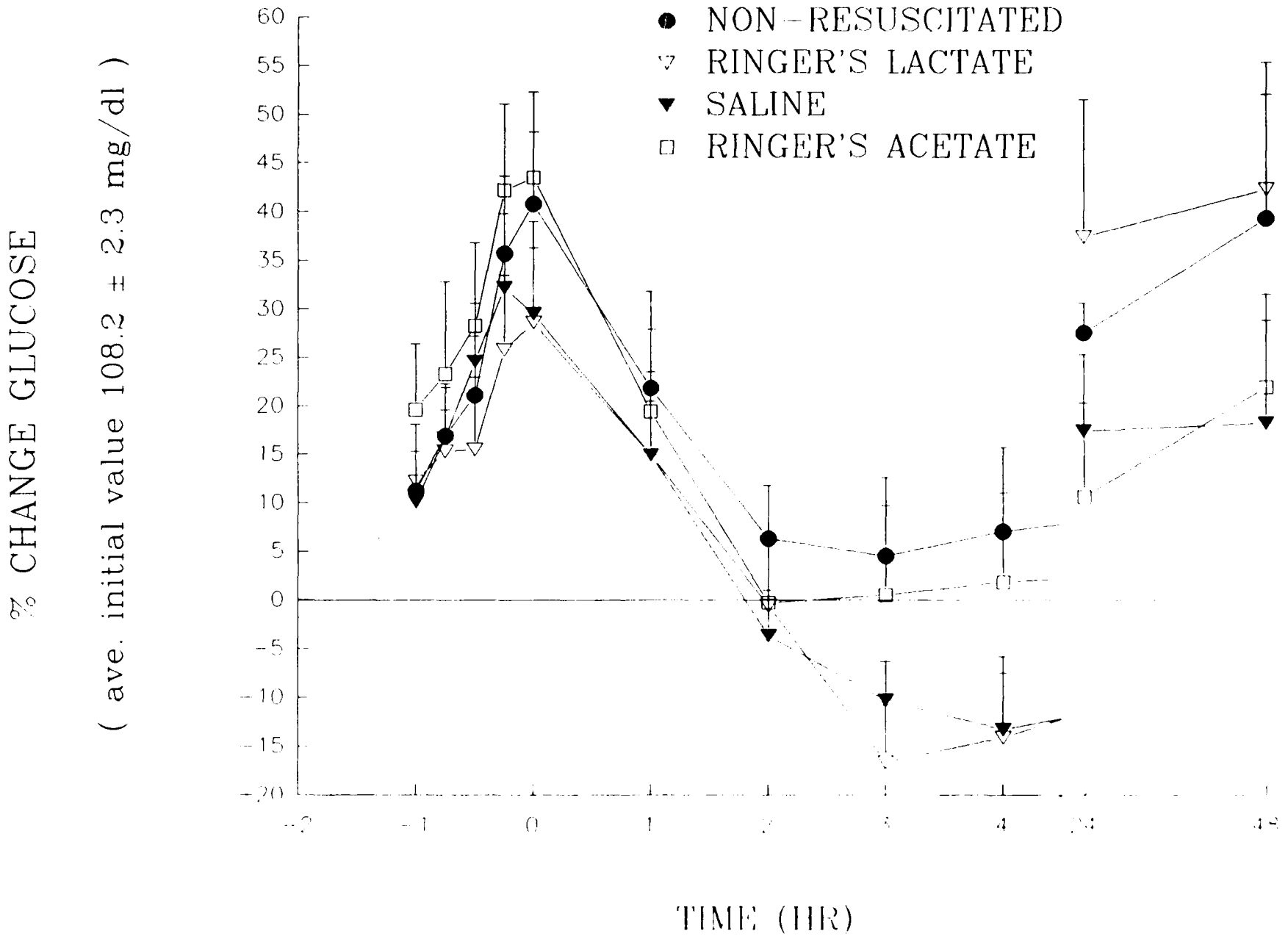

NON-RESUSCITATED
RINGER'S LACTATE
SALINE
RINGER'S ACETATE
% CHANGE GLUCOSE
(ave. initial value 108.2 ± 2.3 mg/dl)
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
-10
-15
-20
-2
-1
0
1
2
3
4
24
48
TIME (HR)

TABLE IV

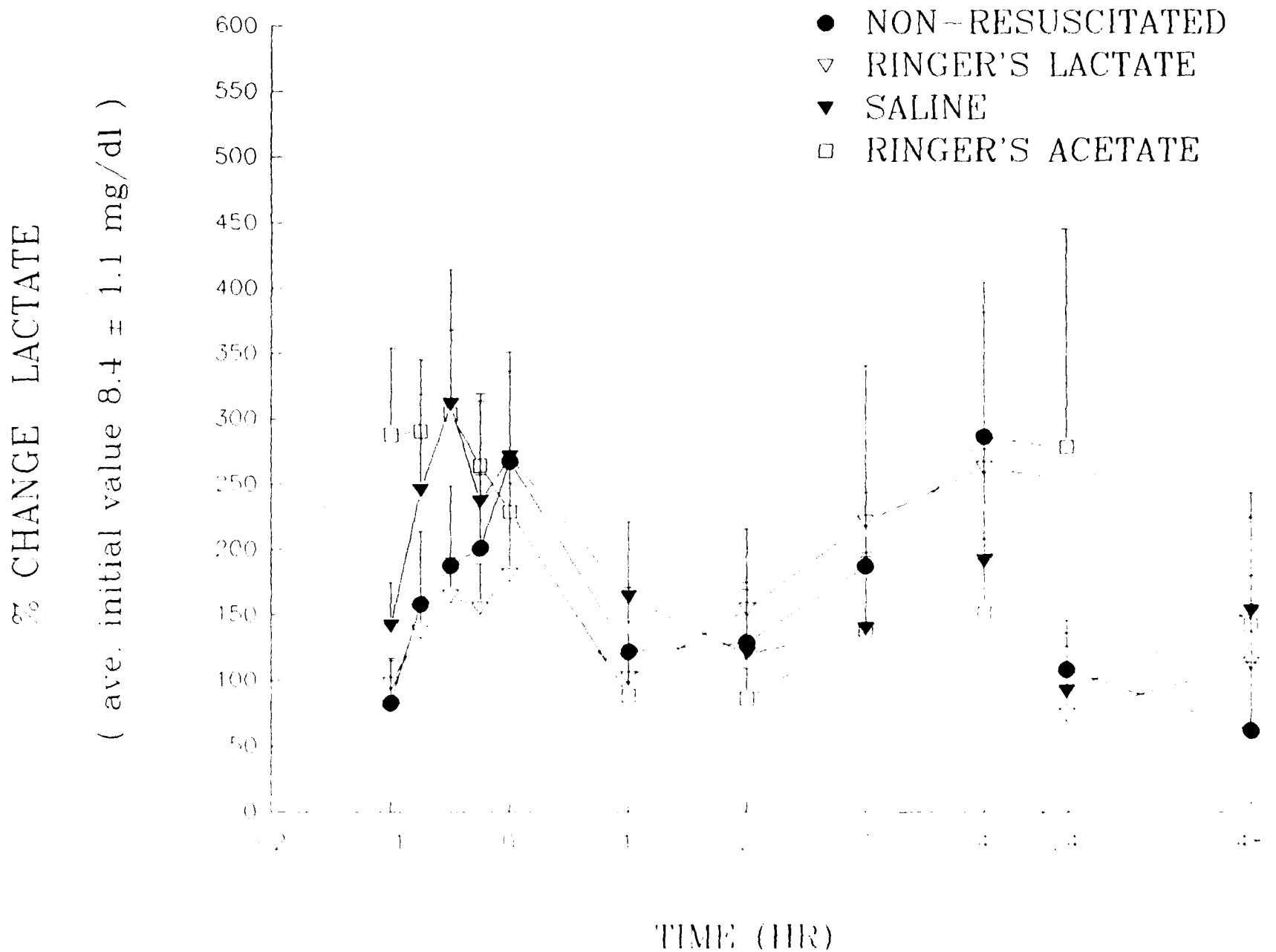
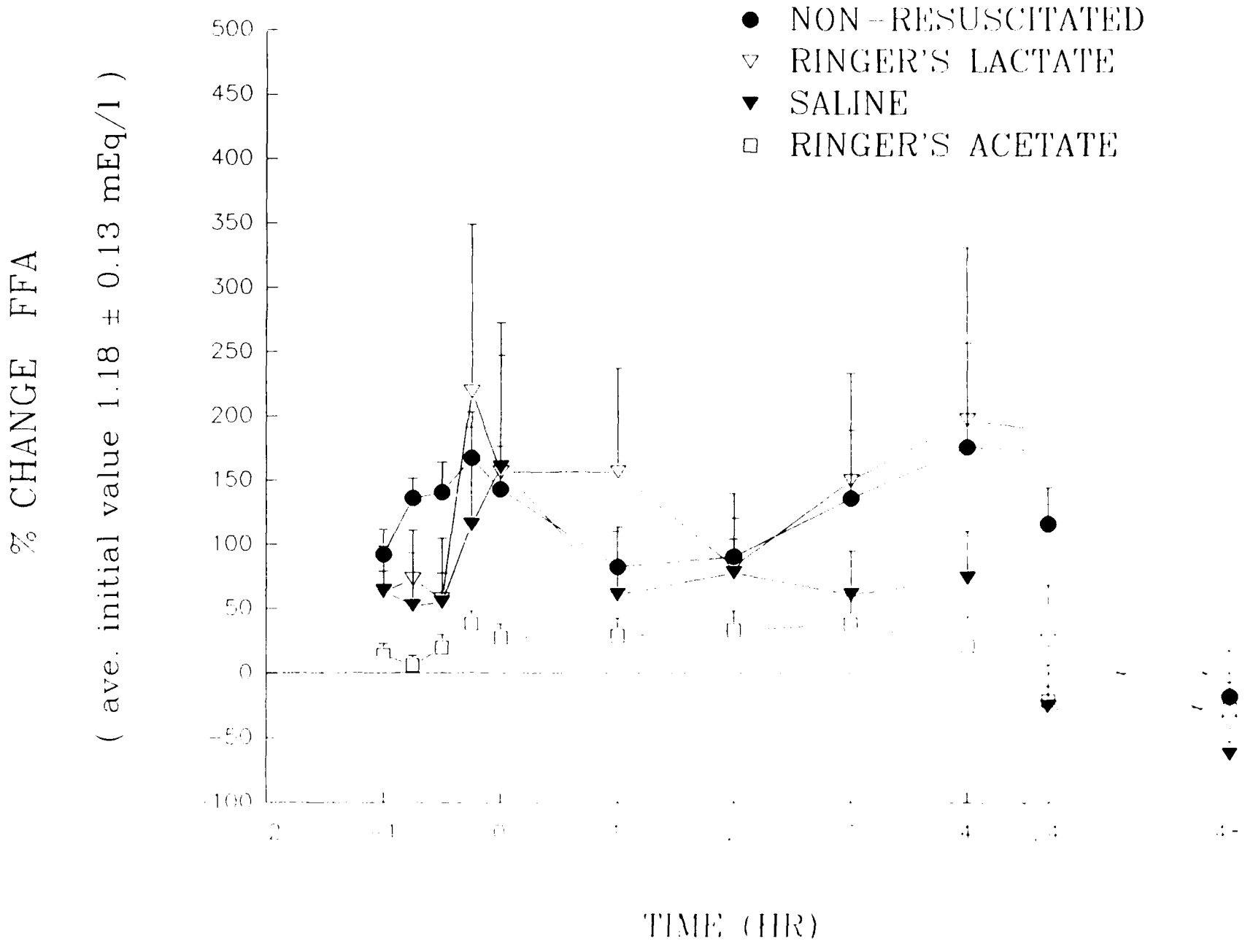

NON-RESUSCITATED
RINGER'S LACTATE
SALINE
RINGER'S ACETATE
% CHANGE LACTATE
(ave. initial value 8.4 = 1.1 mg/dl)
600
550
500
450
400
350
300
250
200
150
100
50
0
TIME (HR)

TABLE V


NON-RESUSCITATED
RINGER'S LACTATE
SALINE
RINGER'S ACETATE
% CHANGE FFA
(ave. initial value 1.18 ± 0.13 mEq/l)
500
450
400
350
300
250
200
150
100
50
0
-50
-100
TIME (HR)